

Int'l Appl. No. : PCT/JP2005/004123
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AMENDMENTS TO THE CLAIMS

1. (Currently amended) A drug for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer, which comprises a lactoferrin hydrolysate as an active ingredient ~~that can be obtained~~obtainable by hydrolyzing lactoferrin with a hydrolytic enzyme and which has an action of enhancing cytotoxic activity of the antibody drug in an antibody therapy of cancer ~~as an active ingredient~~.

2. (Original) The drug according to claim 1, wherein the hydrolytic enzyme is pepsin.

3. (Currently amended) The drug according to claim 1 ~~or 2~~, wherein degradation rate of the lactoferrin hydrolysate is 6 to 20%.

4. (Currently amended) The drug according to ~~any one of claims 1 to 3~~claim 1, wherein the lactoferrin hydrolysate has a number average molecular weight of 500 to 5000.

5. (Currently amended) The drug according to ~~any one of claims 1 to 4~~claim 1, wherein the cancer is any one of breast cancer, B-cell lymphoma or colon cancer.

6. (Currently amended) The drug according to ~~any one of claims 1 to 5~~claim 1, wherein the cancer is a cancer having resistance to the antibody drug.

7. (Currently amended) The drug according to ~~any one of claims 1 to 6~~claim 1, wherein the action of enhancing cytotoxic activity of the antibody drug is an action of increasing ~~sensibility~~sensitivity of target cells to the antibody drug.

8. (Currently amended) A drug for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer, which comprises any one type or a mixture of two or more types of the following peptides of (a) to (d) as an active ingredient:

(a) a peptide having the amino acid sequence of SEQ ID NO: 2;

(b) a peptide having the amino acid sequence of the amino acid numbers 36 to 60 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer;

(c) a peptide having the amino acid sequence of SEQ ID NO: 3;

(d) a peptide having the amino acid sequence of the amino acid numbers 36 to 61 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of

one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer.

9. (Original) The drug according to claim 8, wherein the cancer is any one of breast cancer, B-cell lymphoma or colon cancer.

10. (Currently amended) The drug according to claim ~~8 or 9~~, wherein the cancer is a cancer having resistance to the antibody drug.

11. (Currently amended) The drug according to ~~any one of claims 8 to 10~~ claim 8, wherein the action of enhancing cytotoxic activity of the antibody drug is an action of increasing ~~sensibility~~ sensitivity of target cells to the antibody drug.

12. (Currently amended) Food or drink comprising the drug according to ~~any one of claims 1 to 11~~ claim 1.

13. (Currently amended) Food or drink comprising a lactoferrin hydrolysate ~~that can be obtained~~ obtainable by hydrolyzing lactoferrin with a hydrolytic enzyme and which has an action of enhancing cytotoxic activity of an antibody drug used for an antibody therapy of cancer and attached with an indication that the food or drink is used for enhancing cytotoxic activity of an antibody drug used for an antibody therapy of cancer.

14. (Currently amended) A drug for an antibody therapy of cancer, which comprises a lactoferrin hydrolysate ~~that can be obtained~~ obtainable by hydrolyzing lactoferrin with a hydrolytic enzyme and an antibody drug as active ingredients.

15. (Original) The drug according to claim 14, wherein the hydrolytic enzyme is pepsin.

16. (Currently amended) The drug according to claim ~~14 or 15~~, wherein degradation rate of the lactoferrin hydrolysate is 6 to 20%.

17. (Currently amended) The drug according to ~~any one of claims 14 to 16~~ claim 14, wherein the lactoferrin hydrolysate has a number average molecular weight of 500 to 5000.

18. (Currently amended) The drug according to ~~any one of claims 14 to 17~~ claim 14, wherein the antibody drug is an anti-CD20 antibody, anti-HER2 monoclonal antibody or anti-17-1A (human tumor-related epithelial cell adhesion factor) antibody.

19. (Currently amended) The drug according to ~~any one of claims 14 to 18~~ claim 14, wherein the cancer is a cancer having resistance to the antibody drug.

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20. (Currently amended) A drug for an antibody therapy of cancer, which comprises any one type or a mixture of two or more types of the following peptides of (a) to (d) and an antibody drug as active ingredients:

- (a) a peptide having the amino acid sequence of SEQ ID NO: 2;
- (b) a peptide having the amino acid sequence of the amino acid numbers 36 to 60 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer;
- (c) a peptide having the amino acid sequence of SEQ ID NO: 3;
- (d) a peptide having the amino acid sequence of the amino acid numbers 36 to 61 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer.

21. (Original) The drug according to claim 20, wherein the antibody drug is an anti-CD20 antibody, anti-HER2 monoclonal antibody or anti-17-1A (human tumor-related epithelial cell adhesion factor) antibody.

22. (Currently amended) The drug according to claim 20 ~~or 21~~, wherein the cancer is a cancer having resistance to the antibody drug.

23. (Currently amended) A method of treating cancer comprising administering ~~Use of a~~ lactoferrin hydrolysate ~~that can be obtained~~ obtainable by hydrolyzing lactoferrin with a hydrolytic enzyme ~~and has an action of enhancing~~ in an amount sufficient to enhance cytotoxic activity of an antibody drug in an antibody therapy of cancer to a subject in need thereof ~~for the production of a drug for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer.~~

24. (Currently amended) ~~Use of any one type or a mixture of two or more types of the following peptides of (a) to (d) for the production of a~~ A method of preparing a drug for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer which comprises mixing any one type or a mixture of two or more types of the following peptides (a) to (d) with a pharmaceutically acceptable carrier:

- (a) a peptide having the amino acid sequence of SEQ ID NO: 2;

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(b) a peptide having the amino acid sequence of the amino acid numbers 36 to 60 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer;

(c) a peptide having the amino acid sequence of SEQ ID NO: 3;

(d) a peptide having the amino acid sequence of the amino acid numbers 36 to 61 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer.

25. (Currently amended) A method for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer using the antibody drug, ~~wherein~~ which comprises administering to a patient a lactoferrin hydrolysate ~~that can be obtained~~ obtainable by hydrolyzing lactoferrin with a hydrolytic enzyme and which has an action of enhancing cytotoxic activity of the antibody drug in an antibody therapy of cancer ~~is administered to a patient~~.

26. (Currently amended) A method for enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer using the antibody drug, ~~wherein~~ which comprises administering any one type or a mixture of two or more types of the following peptides of (a) to (d) is administered to a patient:

(a) a peptide having the amino acid sequence of SEQ ID NO: 2;

(b) a peptide having the amino acid sequence of the amino acid numbers 36 to 60 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer;

(c) a peptide having the amino acid sequence of SEQ ID NO: 3;

(d) a peptide having the amino acid sequence of the amino acid numbers 36 to 61 in the amino acid sequence of SEQ ID NO: 1, which includes substitution, deletion, addition or inversion of one or more amino acid residues thereof, and having an action of enhancing cytotoxic activity of an antibody drug in an antibody therapy of cancer.